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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/091,236	03/04/2002	Christine Dingivan	10271-053	7180

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 06/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/091,236	DINGIVAN ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/12/05; 3/31/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-70* is/are pending in the application.

4a) Of the above claim(s) *7,8,12-17,19-21,25-27,32-42,53,55-57 and 63-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9-11,18,22-24,28-31,43-52,54 and 58-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group I and to prosecute the species wherein the alphavbeta3 antagonist is VITAXIN / anti-alphavbeta3 antibody and the TNF-alpha antagonist is REMICADE / anti-TNF-alpha antibody in the Reply, filed 12/1205 and the disease "rheumatoid arthritis" in the Reply, filed 3/31/06, is acknowledged.

Applicant traverses the Restriction Requirement on the grounds that the multiplicity of the species does not require an extensive and burdensome search.

However, this is an election of species not Groups and has been treated as an election of species.

Applicant is reminded of the following with respect to the election of species.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. See MPEP 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Given that applicant does not admit or provide evidence the species are obvious variants, the species requirement is maintained for the reasons of record.

However, upon reconsideration of the elected species "rheumatoid arthritis" in the context of the claimed invention and the prior art search, the examiner has extended the search in the context of treating rheumatoid arthritis with "anti-alphavbeta3 antibodies", as exemplified by the "LM609 / Vitaxin antibody" in combination with "anti-TNFα antibodies", as exemplified by the cA2 / Remicade / infliximab antibody and further in conjunction with standard therapy of treating arthritis with "methotrexate" and "non-steroidal anti-inflammatory drugs" in the interest of compact prosecution.

Claims 1-6, 9-11, 18, 22-24, 28-31, 43-52, 54 and 58-62 are under consideration in the instant application, as they read on the elected invention / species, that is,
"LM609 / Vitaxin antibody" in combination with "anti-TNFα antibodies", as exemplified by the cA2 / Remicade / infliximab antibody and further in conjunction with standard therapy of treating arthritis with "methotrexate" and "non-steroidal anti-inflammatory drugs".

However, claims 7-8, 12-17, 19-21, 25-27, 32-42, 53, 55-57 and 63-70 are drawn to the use of anti-CD2 antibodies, as exemplified by the MEDI-507 antibody, as well as other non-anti-TNFα / anti-alphavbeta3 antibodies recited in the instant claims in addition to the product claims have been withdrawn from consideration as being drawn to non-elected inventions and species.

Also, applicant's (Status Identifiers) that indicated "(Withdrawn)" are misleading, as a number of the claims indicated as "Withdrawn" are under consideration in the instant application.

Applicant is invited to provide a new set of claims indicating the proper status of the pending claims to avoid confusion.

2. Applicant is invited to verify the priority date of the instant claims with respect to written support and enablement under 35 USC 112, first paragraph, to the priority documents.

3. Applicant should amend the first line of the specification to update the proper USSN application number, status and relationship of the priority documents.

4. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the Ô or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.
Appropriate corrections are required

5. Claims 1-6, 9-11, 18, 22-24, 28-31, 43-52, 54 and 58-62 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-6, 9-11, 18, 22-24, 28-31, 43-52, 54 and 58-62 are indefinite in the recitation of "immunomodulatory agents", "anti-inflammatory agents", "immunomodulatory agents is a small organic molecule" because the claims do not apprise the ordinary artisan of the metes and bounds of each of these categories of therapeutic agents.

For example, there is overlap between "immunomodulatory agents" and "immunosuppressive agents".

Further, the claims have recited alphavbeta3 antagonists and TNF antagonists as separate categories, yet the ordinary artisan would ascribe both "immunomodualtory and immunosuppressive properties to such antagonists.

The term "immunodulatory" is relative in nature and does not apprise the ordinary artisan of the nature, direction or type of "modulation" encompassed by the claimed invention.

Applicant is invited to amend the claims to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

For example, applicant is invited to recite specific "agents" or defined categories of agents that would reasonably apprise the ordinary artisan of the claimed invention, particularly as it reads on what appears to be overlapping categories of therapeutic molecules.

B) Claims 2, 4, 6, 9-11, 18, 22-24, 28-31, 43-46-54 and 58-62 are indefinite in the recitation of "VITAXIN" and "REMICADE " because their characteristics are not known. The use of "VITAXIN", "REMICADE" as the sole means of identifying the claimed antibodies renders the claims indefinite because these are merely laboratory designations which do not clearly define the claimed products, since different laboratories may use the same laboratory designations to define completely distinct cell lines .

Amending the claims to recite the appropriate ATCC Accession Numbers would obviate this rejection.

C) Claims 2, 4, 6, 9-11, 18, 22-24, 28-31, 43-46-54 and 58-62 contain the trademark or trade name "VITAXIN", "REMICADE" (and non-elected "ENBREL") . Where a trademark or trade name is used in a claims as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 USC 112, second paragraph, See Ex parte Simpson, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademarks or the trade names are used to identify or describe "antibodies", and accordingly, the identification or the description is indefinite. The relationship between a trademark or tradename and the product it identifies may be uncertain and arbitrary. The formula or characteristics of the product may change from time to time and yet it may continue to be sold under the same trademark or tradename.

D) Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 2, 4, 6, 9-11, 18, 22-24, 28-31, 43-46-54 and 58-62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

It is apparent that the "VITAXIN" and "REMICADE" antibodies are required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the pertinent cell lines / hybridomas which produce these antibodies. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

Applicant is invited to clarify the record for the public availability of the claimed "VITAXIN" / "REMICADE" antibodies with respect to the requirements for the deposit of biological materials under 35 UWC 112, first paragraph. See MPEP 2400.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-6, 9-11, 18, 22-24, 28-31, 43-52, 54 and 58-62 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Feldman et al. (U.S. Patent NO. 6,270,766) in view of by Huse (U.S. Patent No. 6,596,850), The Merck Manual of Diagnosis and Therapy, Seventeenth Edition, edited by Beers et al., Merck Research Laboratories, Whitehouse Station, NJ, 1999 (see pages 416-423) and Strom et al. (in Therapeutic Immunology edited by Austen et al., Blackwell Science, Cambridge, MA, 1996; see pages 451-456).

Feldmann et al. teach the use of anti-TNFα antibodies, including the cA2 antibody as well as various recombinant forms of antibodies and antigen-binding fragments (e.g. see Anti-TNF Antibodies on columns 7-16) in combination with methotrexate, prior to simultaneously of sequentially with one another (e.g. see columns 18-20, Methotrexate and Administration). Here, other therapeutic regimens or agents can be used in combination with the therapeutic administration of TNF antagonists and methotrexate are taught in order to maintain the reduction or elimination of signs associated with a particular TNF-mediated disease (e.g. see Administration on column 18-20).

For examination purposes, it is pointed out that the recombinant cA2 anti-TNFα antibody is Remicade.

Feldman et al. differs from the claimed methods by not describing all of the current methods of treating rheumatoid arthritis, as referenced herein by The Merck Manual as well as the use of alphavbeta3-specific antibodies in the treatment of rheumatoid arthritis.

Huse teaches various diseases, including rheumatoid arthritis (e.g. see column 25, lines 64) with effective amounts alphvabeta3-specific antibodies, including Vitaxin, a LM609 grafted antibody and antigen binding fragments thereof (e.g. see column 26, paragraphs 1-4) (see entire document). A full description of the alphvabeta3-specific antibodies, including Vitaxin, a LM609 grafted antibody and antigen binding fragments thereof are set forth in columns 4-24). Huse teaches modes of administration and effective dosages encompassed by the claimed methods in order to meet the needs of the patient (e.g. see column 26, paragraph 1 – column 27, paragraph 1). Here, too, Huse teaches co-administration with other compositions to enhance or supplement the treatment of an alphavbeta3 disease (e.g. see column 26, paragraph 2)

The Merck Manual describes the known treatments for rheumatoid arthritis, including nonsteroidal anti-inflammatory drugs and salicylates as well as methotrexate and cortiocosteroids (see entire document, particularly Treatment on pages 419-423). The Merck Manual also notes that combinations may be more effective than single drugs (e.g. see page 421, columns 2, Combinations of slow-acting drugs).

Strom et al. teach that it was known and practiced by the ordinary artisan to employ a multitiered approach to immunosuppressive therapy similar in principle to that used in chemotherapy, several agents are used simultaneously, each of which is directed to a different molecular targets. Additive-synergistic effects are achieved through application of each agent at relatively low dose, thereby limiting the toxicity of each individual agent while increasing the total immunosuppressive effect (see entire document, including the introduction on page 451).

Given the combined teachings, one of ordinary skill in the art at the time the invention was made would have been motivated and would have had a reasonable expectation of success of providing multiple immunosuppressive agents in the treatment of rheumatoid arthritis, as commonly practiced at the time the invention was made, and as taught by the primary and secondary references. Also, it is noted that the teachings of both Feldman et al. and Huse are consistent with this common practice, as both teachings teach combination therapies with either TNFα antagonists such as anti-TNFα antibodies or alphavbeta3 antagonists such as anti-alphavbeta3 antibodies, including their combination with known therapeutic regimens for the disease targeted.

Also, it was prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

It appears that the claimed limitations were well within the purview of an ordinary artisan at the time the invention was made. The various dosages and modes of administration encompassed by the claimed methods (e.g. see claims 31, 50-54 and 59-62) appear to the same or nearly the same as set above, particularly in the teachings of Feldman et al. (e.g. see Administration on column 18, to meet the needs of the patient and the particular disease. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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